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EXAMINER
DIAMOND, ALAN D

ART UNIT	PAPER NUMBER
1753	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/052,601	ROBERT, FREDERIC	
	Examiner	Art Unit	
	Alan Diamond	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 March 2006 and 27 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,8-25 and 30-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,8-25 and 30-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Comments

1. The objection to the specification under 35 USC 132(a) has been overcome by Applicant's amendment of the specification.

2. The objection to the abstract has been overcome by Applicant's amendment of the abstract.

3. The rejection of claim 18 under 35 USC 112, second paragraph, has been overcome by Applicant's amendment of the claim.

Claim Objections

4. Claims 1 and 30-32 are objected to because of the following informalities:

In claim 1 at line 4, in claim 31 at line 17, and in claim 32 at line 4, the "a_1" and "a_2" should be changed to "α_1" and "α_2" respectively.

In each of independent claims 1, 30, 31, and 32, there are several locations in chemical names of the buffers where the letter "l" should be changed to the number "1". These location with the change that needs to be made are as follows: In claim 1 at line 9, change "l, 3" to "1, 3"; in claim 1 at line 11, change "l, 1" to "1, 1"; in claim 1 at line 13 change "hydroxy-l-" to "hydroxy-1-"; in claim 1 at the end of line 14 change "cyclohexylamino-l-" to "cyclohexylamino-1-"; in claim 30 at line 9 change "l, 3" to "1, 3"; in claim 30 at line 10, change "l, 1" to "1, 1"; in claim 30 at line 13 change "hydroxy-l-" to "hydroxy-1-"; in claim 30 at the end of line 14 change "cyclohexylamino-l-" to "cyclohexylamino-1-"; in claim 31 at line 7, change "l, 3" to "1, 3"; in claim 31 at line 8, change "l, 1" to "1, 1"; in claim 31 at line 11 change "hydroxy-l-" to "hydroxy-1-"; in claim

31 at the end of line 12 change "cyclohexylamino-l-" to "cyclohexylamino-1-"; in claim 32 at line 9, change "l, 3" to "1, 3"; in claim 32 at line 11, change "l, 1" to "1, 1"; in claim 32 at line 13 change "hydroxy-l-" to "hydroxy-1-"; in claim 32 at the end of line 14 change "cyclohexylamino-l-" to "cyclohexylamino-1-";

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 31 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 31 is indefinite because it is not clear how the method comprises analyzing or separating serum protein constituents selected from albumin, a_1-globulin, a_2-globulin, β-globulin, β_1-globulin, β_2-globulin and γ-globulin when none of these proteins is positively recited as being introduced into the capillary tube during the "introducing" step.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1, 3, 8-11, 16-19, 21-25, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keo et al in (U.S. Patent 5,599,433) view of Lehninger, Principles of Biochemistry, pp. 706-707, (1982) and Lau (U.S. Patent 5,194,390).

Keo et al teaches the capillary zone electrophoresis (CZE) of glycosylated proteins in clinical specimens from humans, wherein the buffer system contains, for example, 100 mM CAPS (which reads on the instant biological buffer), 300 mM sodium borate (which reads on the instant additive that increases ionic strength), and NaOH for adjusting the pH to 11 (see col. 1, lines 19-23; col. 3, lines 32-55; col. 4, lines 43-49; col. 5, line 16 through col. 6, line 14; and col. 8, lines 32-43). The sodium borate concentration can be 50 to 200 mM (see col. 5, lines 43-65). The clinical specimen can be a human biological liquid such as serum, plasma, cerebrospinal fluid, urine, etc (see col. 6, lines 17-22). With respect to claims 18 and 19, said CAPS is a C_9 alkylsulfonate. With respect to claim 21, and as noted above, the CAPS has a concentration of 100 mM. Thus, for example, 1 mm or 5 mM of the 100 mM CAPS corresponds to the 1 to 5 mM alkylsulfonate in claim 21, while the remaining 99 mM or 95 mM CAPS corresponds to the instant buffer. Keo et al teaches the limitations of the limitations of the instant claims other than the differences which are discussed below.

Keo et al does not specifically require that said buffer system containing, for example, 100 mM CAPS, 300 mM sodium borate, and NaOH be used for the serum, plasma, cerebrospinal fluid, or urine biological fluid. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used said buffer system containing 100 mM CAPS, 300 mM sodium borate, and NaOH

for the serum, plasma, cerebrospinal fluid, or urine biological fluid because such is clearly within the scope of Keo et al's disclosure.

With respect to claim 1 and its dependent claims, Keo et al does not specifically teach that its clinical sample contains the instant protein constituent. As noted above, Keo et al teaches that its clinical sample can be human plasma or urine. Lehninger is relied upon for showing that over 70% of the plasma solids in blood plasma is attributed by the plasma proteins listed in Table 24-3 at page 707, and include the instant albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins. Lau is relied upon for teaching what is well known, i.e., that approximately one third of total urinary protein is serum albumin (see col. 1, lines 52-57). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used plasma or urine as Keo et al's clinical sample because such is clearly within the scope of Keo et al's disclosure. Over 70% of the plasma solids in blood plasma is attributed by the plasma proteins listed in Table 24-3 at page 707 of Lehninger, and include the instant albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins. Furthermore, approximately one third of total urinary protein is serum albumin, as shown by Lau.

With respect to claim 32, it is noted that this claim recites that "said buffer system does not contain borate". However, Keo et al does not require that its complexing agent be borate (see abstract; col. 3, lines 25-55; and claim 1 at cols. 9-10). Indeed, Keo et al's claim 1 recites a complexing agent, but does not recite or require borate. Borate is an example, of Keo et al's complexing agent. It would have been well within the skill of

an artisan to have used a suitable complexing agent, other than borate, for Keo et al's complexing agent because such is clearly within the scope of Keo et al's disclosure.

9. Claims 2 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keo et al in view of Lehninger and Lau as applied to claims 1, 3, 8-11, 16-19, 21-25, and 32 above, and further in view of Krylov et al, "Capillary Electrophoresis for the Analysis of Biopolymers," Anal. Chem., pages 111R-128R (2000).

Keo et al in view of Lehninger and Lau is relied upon for the reasons recited above. With respect to claims 2 and 31, Keo et al teaches that that, using the CZE, the glycoproteins are separated from any other proteins in the sample (see col. 3, lines 59-62). As noted above, albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins are in plasma, and serum albumin is in urine. Accordingly, using the CZE, said albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins are separated from the glycoproteins when the sample is plasma, and serum albumin is separated from the glycoproteins when the sample is urine. Thus, the requirement in instant claims 2 and 31 of "separating" is achieved when Keo et al performs the CZE on the plasma or urine. With respect to the requirement of "detecting said protein constituents" in claim 2, Keo et al teaches that the electrophoretically separated proteins are detected by a suitable method, such as measurement of light absorption at 415 nm. The detection of proteins is conventional in the art. Indeed, Krylov et al teaches that UV absorption can be used to detect proteins, and, in Table 1 at the bottom of page 116R shows that UV absorbance has been used to detect human plasma proteins when separated by CZE (see also the Detection section at pages 118R-124R). It would have been obvious to

one of ordinary skill in the art at the time the invention was made to have detected the plasma proteins after Keo et al's separation because detection of proteins is well known in the art, and, indeed, Krylov et al teaches that UV absorption can be used to detect proteins and shows that UV absorbance has been used to detect human plasma proteins when separated by CZE. With respect to claim 31, when the proteins are detected that are also analyzed.

10. Claims 12-14 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keo et al in view of Lehninger and Lau as applied to claims 1, 3, 8-11, 16-19, 21-25, and 32 above, and further in view of Swank et al (U.S. Patent 4,810,657).

Keo et al in view of Lehninger and Lau, as relied upon for the reasons recited above, teaches the limitations of claims 12-14 and 30, the difference being that Keo et al does not specifically teach the presence of, for example, sodium chloride, in its buffer system. Swank et al is relied upon for showing what is well known, i.e., that sodium chloride is a constituent of blood plasma (see col. 4, lines 12-13). Thus, by performing Keo et al's capillary zone electrophoresis on blood plasma, sodium chloride will be introduced into the buffer due to the fact that blood plasma contains sodium chloride. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have sodium chloride present in Keo et al's buffer because when Keo et al's capillary zone electrophoresis is performed on blood plasma, sodium chloride will be introduced into the buffer from the blood plasma, which contains sodium chloride, as taught by Swank et al.

11. Claims 12-15 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keo et al in view of Lehninger and Lau as applied to claims 1, 3, 8-11, 16-19, 21-25, and 32 above, and further in view of Lehninger, Principles of Biochemistry, p. 703, (1982).

Keo et al in view of Lehninger and Lau, as relied upon for the reasons recited above, teaches the limitations of claims 12-15 and 30, the difference being that Keo et al does not specifically teach the presence of sodium sulfate in its buffer system. Page 703 of Lehninger relied upon for showing what is well known, i.e., that sodium sulfate is a constituent of urine (see Table 24-2), and is present in the urine due to the presence of Na^+ and SO_4^{2-}. Thus, by performing Keo et al's capillary zone electrophoresis on urine, sodium sulfate will be introduced into the buffer due to the fact that urine contains sodium sulfate. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have sodium sulfate present in Keo et al's buffer because when Keo et al's capillary zone electrophoresis is performed on urine, sodium sulfate will be introduced into the buffer from the urine, which contains sodium sulfate, as taught by Lehninger.

12. Claims 1, 3, 8-14, 16-25, 30, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keo et al in (U.S. Patent 5,599,433) view of Lehninger, Principles of Biochemistry, pp. 706-707, (1982), Lau (U.S. Patent 5,194,390), and Jones et al (U.S. Patent 5,366,601).

Keo et al teaches the capillary zone electrophoresis (CZE) of glycosylated proteins in clinical specimens from humans, wherein the buffer system contains, for

example, 100 mM CAPS (which reads on the instant biological buffer), 300 mM sodium borate (which reads on the instant additive that increases ionic strength), and NaOH for adjusting the pH to 11 (see col. 1, lines 19-23; col. 3, lines 32-55; col. 4, lines 43-49; col. 5, line 16 through col. 6, line 14; and col. 8, lines 32-43). The sodium borate concentration can be 50 to 200 mM (see col. 5, lines 43-65). The clinical specimen can be a human biological liquid such as serum, plasma, cerebrospinal fluid, urine, etc (see col. 6, lines 17-22). With respect to claims 18 and 19, said CAPS is a C_9 alkylsulfonate. With respect to claim 21, and as noted above, the CAPS has a concentration of 100 mM. Thus, for example, 1 mm or 5 mM of the 100 mM CAPS corresponds to the 1 to 5 mM alkylsulfonate in claim 21, while the remaining 99 mM or 95 mM CAPS corresponds to the instant buffer. Keo et al teaches the limitations of the limitations of the instant claims other than the differences which are discussed below.

Keo et al does not specifically require that said buffer system containing, for example, 100 mM CAPS, 300 mM sodium borate, and NaOH be used for the serum, plasma, cerebrospinal fluid, or urine biological fluid. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used said buffer system containing 100 mM CAPS, 300 mM sodium borate, and NaOH for the serum, plasma, cerebrospinal fluid, or urine biological fluid because such is clearly within the scope of Keo et al's disclosure.

With respect to claim 1 and its dependent claims, Keo et al does not specifically teach that its clinical sample contains the instant protein constituent. As noted above, Keo et al teaches that its clinical sample can be human plasma or urine. Lehninger is

relied upon for showing that over 70% of the plasma solids in blood plasma is attributed by the plasma proteins listed in Table 24-3 at page 707, and include the instant albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins. Lau is relied upon for teaching what is well known, i.e., that approximately one third of total urinary protein is serum albumin (see col. 1, lines 52-57). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used plasma or urine as Keo et al's clinical sample because such is clearly within the scope of Keo et al's disclosure. Over 70% of the plasma solids in blood plasma is attributed by the plasma proteins listed in Table 24-3 at page 707 of Lehninger, and include the instant albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins. Furthermore, approximately one third of total urinary protein is serum albumin, as shown by Lau.

With respect to claims 12-14 and 20, Keo et al does not specifically teach that its buffer contains an additive such as sodium octanesulfonate (see col. 7, lines 15-35). Jones et al teaches the capillary zone electrophoresis of anionic species, wherein sodium octanesulfonate is used in the buffer as an electromigration agent. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have added the sodium octanesulfonate to Keo et al's capillary zone electrophoresis buffer so as to take advantage of the sodium octanesulfonate's known function in capillary zone electrophoresis, i.e., as an electromigration aid, as taught by Jones et al.

13. Claims 2 and 31 rejected under 35 U.S.C. 103(a) as being unpatentable over Keo et al in view of Lehninger, Lau, and Jones et al as applied to claims 1, 3, 8-14, 16-

25, 30, and 32 above, and further in view of Krylov et al, "Capillary Electrophoresis for the Analysis of Biopolymers," Anal. Chem., pages 111R-128R (2000).

Keo et al in view of Lehninger and Lau is relied upon for the reasons recited above. With respect to claims 2 and 31, Keo et al teaches that that, using the CZE, the glycoproteins are separated from any other proteins in the sample (see col. 3, lines 59-62). As noted above, albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins are in plasma, and serum albumin is in urine. Accordingly, using the CZE, said albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins are separated from the glycoproteins when the sample is plasma, and serum albumin is separated from the glycoproteins when the sample is urine. Thus, the requirement in instant claims 2 and 31 of "separating" the protein constituents is achieved when Keo et al performs the CZE on the plasma or urine. With respect to the requirement of "detecting said protein constituents" in claim 2, Keo et al teaches that the electrophoretically separated proteins are detected by a suitable method, such as measurement of light absorption at 415 nm. The detection of proteins is conventional in the art. Indeed, Krylov et al teaches that UV absorption can be used to detect proteins, and, in Table 1 at the bottom of page 116R shows that UV absorbance has been used to detect human plasma proteins when separated by CZE (see also the Detection section at pages 118R-124R). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have detected the plasma proteins after Keo et al's separation because detection of proteins is well known in the art, and, indeed, Krylov et al teaches that UV absorption can be used to detect proteins and shows that UV absorbance has been used to detect

human plasma proteins when separated by CZE. With respect to claim 31, when the proteins are detected that are also analyzed.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1-3, 8-25, and 30-32 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 4, 5, 7-25, 27-30, and 33-35 of copending Application No. 10/052,931. Although the conflicting claims are not identical, they are not patentably distinct from each other because in claim 23 of said copending application, the buffer can be a zwitterionic biological buffer. As seen in the specification of said copending application the "zwitterionic biological buffer" encompasses buffers such as CAPS.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

16. Applicant's arguments filed March 6, 2006 have been fully considered but they are not persuasive.

Applicant cites col. 5, lines 18-21, of Keo et al and argues that Keo et al is strictly limited to using its buffer system for facilitating the separation of glycoproteins such as Hb Alc from other sample constituents. Applicant argues that there is no disclosure in Keo et al that its method would be able to separate albumin, α_1-globulin, α_2-globulin, β-globulin, β_1-globulin, β_2-globulin and γ-globulin. However, this argument is not deemed to be persuasive. Firstly, the recitation "for analyzing or separating" at line 2 in each of claims 1, 31 and 32, and the recitation "for analyzing" at line 2 of claim 30 is merely intended use of the method and is not deemed to be a positive limitation of these claims. Indeed, the only positively recited step in each of independent claims 1, 30, and 32 is the step of "introducing" the clinical sample into the capillary column, which is precisely what Keo et al does. In any event, Keo et al does analyze or separate a clinical sample comprising serum protein constituents selected form the recited protein constituents. For example, Keo et al's plasma sample, which contains the instant samples, is analyzed for glycoprotein, and the glycoproteins are separated from the other proteins in the clinical sample. Thus, Keo et al's method is one "for analyzing and separating a clinical sample" which comprises the instantly claimed proteins.

Instant claim 2 does recite positive steps of "separating said protein constituents by migration and detecting said protein constituents." Claim 31 recites "analyzing or separating serum protein constituents selected albumin, a_1-globulin, a_2-globulin, β-globulin, β_1-globulin, β_2-globulin and γ-globulin". However, the term "separating" is so

broad that is can be interpreted to mean what Keo et al is doing, i.e., separating the albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins that are in the plasma from the glycoproteins so that the glycoproteins can be analyzed. With respect to the "detecting said protein constituents", it is nothing new to detect proteins in a sample using UV. The albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins, which have been separated from the glycoproteins, can be detected by conventional UV. For example, if the albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins are present as being mixed together in a single fraction from the Keo et al's CZE, they can be detected (as total protein) in the fraction by conventional UV. As noted above, Krylov et al teaches that UV absorption can be used to detect proteins and shows that UV absorbance has been used to detect human plasma proteins when separated by CZE. When proteins are detected, the are also analyzed, as here claimed.

Applicant argues that "the reliance of the Patent Office on the proposition that the clinical samples in Keo et al inherently contain albumin or α_1-globulin, α_2-globulin, β-globulin, β_1-globulin, β_2-globulin and γ-globulin as support for this rejection is misguided." However, this argument is not deemed to be persuasive because Lehninger, as set forth above, has been relied upon for showing that over 70% of the plasma solids in blood plasma is attributed by the plasma proteins listed in Table 24-3 at page 707, and include the instant albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins. Lau, as also set forth above, has been relied upon for teaching what is well known, i.e., that approximately one third of total urinary protein is serum albumin (see col. 1, lines 52-57). The Examiner maintains that it would have been obvious to one of

ordinary skill in the art at the time the invention was made to have used plasma or urine as Keo et al's clinical sample because such is clearly within the scope of Keo et al's disclosure. Over 70% of the plasma solids in blood plasma is attributed by the plasma proteins listed in Table 24-3 at page 707 of Lehninger, and include the instant albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins. Furthermore, approximately one third of total urinary protein is serum albumin, as shown by Lau.

Applicant argues that "the present invention's technique results in the visualization of five peaks in the electropherogram at 10 minutes after applying an electric field." However, this argument is not deemed to be persuasive because the instant claims are silent concerning such peaks, and nothing unexpected with respect to Keo et al and commensurate in scope with the instant claims has been demonstrated.

Applicant argues that there is no suggestion in Keo et al to alter its voltage and time parameters at col. 8, lines 51-53, to obtain a different result for any other protein analysis. However, this argument is not deemed to be persuasive because the instant claims are silent concerning voltage and time. As note above, the only positively recited step in each of independent claims 1, 30, and 32 is the step of "introducing" the clinical sample into the capillary column, which is precisely what Keo et al does. Claim 31 recites "analyzing or separating serum protein constituents selected albumin, a_1-globulin, a_2-globulin, β-globulin, β_1-globulin, β_2-globulin and γ-globulin". However, the term "separating" is so broad that is can be interpreted to mean what Keo et al is doing, i.e., separating the albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins that are in the plasma from the glycoproteins so that the glycoproteins can be analyzed.

Applicant argues that in Keo et al, the sugar complexing agent borate is the agent of choice and must be present, and that the instant invention does not use borate. However, this argument is not deemed to be persuasive. Firstly, the comprising language in each of independent claims 1, 30, and 31 does not exclude the complexing agent of Keo et al. While it is noted that claim 32 recites that "said buffer system does not contain borate", it is noted that Keo et al does not require that its complexing agent be borate (see abstract; col. 3, lines 25-55; and claim 1 at cols. 9-10). Indeed, Keo et al's claim 1 recites a complexing agent, but does not recite or require borate. Borate is an example, of Keo et al's complexing agent. It would have been well within the skill of an artisan to have used a suitable complexing agent, other than borate, for Keo et al's complexing agent because such is clearly within the scope of Keo et al's disclosure.

Applicant provides arguments concerning inherency of Keo et al's clinical samples containing the albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins. However, these arguments are not deemed to be persuasive because Keo et al teaches that its clinical sample can be human plasma or urine. Lehninger is relied upon for showing that over 70% of the plasma solids in blood plasma is attributed by the plasma proteins listed in Table 24-3 at page 707, and include the instant albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins. Lau is relied upon for teaching what is well known, i.e., that approximately one third of total urinary protein is serum albumin (see col. 1, lines 52-57). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used plasma or urine as Keo et al's clinical sample because such is clearly within the scope of Keo et al's disclosure. Over 70% of the

plasma solids in blood plasma is attributed by the plasma proteins listed in Table 24-3 at page 707 of Lehninger, and include the instant albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins. The instant albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins are present in human plasma and urine.

Applicant argues that Lehninger and Lau do not disclose anything about electrophoresis. However, this argument is not deemed to be persuasive because Keo et al teaches the electrophoresis.

Applicant argues that Krylov et al does not remedy the deficiencies of the primary reference, Keo et al, that there is no motivation or suggestion to combine Krylov et al with Keo et al, there is no motivation for one skilled in the art to use the buffer in Keo et al in the procedure of Krylov et al, and that "[s]ince there is absolutely no teaching or suggestion in Keo et al that their CAPS buffer is useful to separate other proteins using capillary electrophoresis, there is no reason to combine the use of Keo et al's buffer with a different capillary electrophoresis technique, such as the ones disclosed in Krylov et al." However, these arguments are not deemed to be persuasive. Krylov et al is a review article of capillary electrophoresis for the analysis and separation of biopolymers. A skilled artisan would use Keo et al's buffer for Keo et al's procedure, and would follow the capillary zone electrophoresis procedures in Krylov et al's Table 1 at page 116R when those procedures are performed. The issue here is what is well known and conventional in the art with respect to the detection of proteins. Krylov et al has been relied upon for showing what is very well known and conventional in the art, i.e., that detection of proteins is conventional. Indeed, Krylov et al teaches that UV absorption

can be used to detect proteins, and, in Table 1 at the bottom of page 116R shows that UV absorbance has been used to detect human plasma proteins when separated by CZE (see also the Detection section at pages 118R-124R). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have detected the plasma proteins after Keo et al's separation because detection of proteins is well known in the art, and, indeed, Krylov et al teaches that UV absorption can be used to detect proteins and shows that UV absorbance has been used to detect human plasma proteins when separated by CZE. With respect to claim 31, when the proteins are detected that are also analyzed.

Applicant argues that claims 12-15 and 30 are directed to additives and not to a substance already present in the clinical sample. However, this argument is not deemed to be persuasive because before the sample volume is completely injected in the column, some of the sample will be in the column and some will be in the injector. The sample in the column is mixed with Keo et al's buffer in the column, and thus, there will be sodium chloride or sodium sulfate in the buffer before the sample is completely injected into the column.

Applicant argues that Jones et al does not disclose that octanesulfonate can be used in a process other than with ionic molecules. However, this argument is not deemed to be persuasive because proteins are ionic.

Applicant argues that there is no suggestion that octanesulfonate can be used as an additive in a migration system to improve the separation of albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulin. However, this argument is not deemed to be

persuasive because the only positively recited step in each of independent claims 1, 30, and 32 is the step of "introducing" the clinical sample into the capillary column, which is precisely what Keo et al does. Claim 31 recites "analyzing or separating serum protein constituents selected albumin, a_1-globulin, a_2-globulin, β-globulin, β_1-globulin, β_2-globulin and γ-globulin". However, the term "separating" is so broad that is can be interpreted to mean what Keo et al is doing, i.e., separating the albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins that are in the plasma from the glycoproteins so that the glycoproteins can be analyzed. The Examiner maintains that it would have been obvious to one of ordinary skill in the art at the time the invention was made to have added the sodium octanesulfonate to Keo et al's capillary zone electrophoresis buffer so as to take advantage of the sodium octanesulfonate's known function in capillary zone electrophoresis, i.e., as an electromigration aid, as taught by Jones et al.

The Examiner notes that independent claims 31 and 32 have been added to the instant application. However, for the reasons set forth above, these claims are not patentable over the art.

Conclusion

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alan Diamond whose telephone number is 571-272-1338. The examiner can normally be reached on Monday through Friday, 5:30 a.m. to 2:00 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen can be reached on 571-272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alan Diamond
June 10, 2006

Alan Diamond
Primary Examiner
Art Unit 1753